REMARKS

The amendments to the specification add references to SEQ ID NOs for sequences presented in Figure 8 and Figure 10. Particularly, the amino acid sequence designated MU12A is properly referred to as SEQ ID NO: 19 at page 25 of the specification. Additionally, this sequence designated MU12A-HIS is referred to as SEQ ID NO: 21 at page 25 of the specification. Support for this amendment can be found in the Sequence Listing and in Figures 8 and 10. Additionally, this amendment is made in an effort to comply with the sequence listing requirements set forth in 37 C.F.R § 1.821 et seq. Accordingly, no new matter has been added.

The amendments to the claims as set forth above are intended to more particularly point out and distinctly claim the subject invention. Support for the amendments can be found in the specification, Sequence Listing, and claims as originally filed. For example, the amendment to claim 12 reciting a bovine gamma-II-crystalline is supported by the Sequence Listing, in which SEQ ID NOs: 19-22 are identified as being from *Bos sp.* Support for this amendment can also be found in the first Example in the English translation of the specification, in which a bovine gamma-B-crystalline (gamma-II) is disclosed.

New claims 26-45 have been added. These claims are also intended to more particularly point out and distinctly claim the subject invention. Support for the new claims can also be found in the claims as originally filed, at page 4-5 of the specification, and in the Examples. Below is a Table that points out additional support for each of the newly added claims. No new matter has been added by any of the claim amendments or the new claims.

New Claim No.	Support
26	Claim 7
27	Claim 10
28	Claim 11
29	Claim 20(d)
30	Claim 22
31	Claim 21; page 8 of the English translation of the specification (definition of "mutagenization")
32	Claim 21; page 8 of the English translation of the specification (definition of "mutagenization")
33	Claim 21; page 8 of the English translation of the specification (definition of "mutagenization")
34	Claim 21; page 8 of the English translation of the specification (definition of "mutagenization")
35	Claim 21; page 8 of the English translation of the specification (definition of "mutagenization")
36	Claim 19

37	Claim 19
38	Claim 19
39	Claims 19 and 15
40	Claim 19
41	Claims 19 and 15
42	Claims 8, 13, 17, and 21; page 8 of the English translation of the specification (definition of "mutagenization")
43	Claims 8, 13, 17, and 21; page 8 of the English translation of the specification (definition of "mutagenization")
44	Claims 8, 13, 16, 17, and 21; page 8 of the English translation of the specification (definition of "mutagenization")
45	Page 8 of the English translation of the specification (definition of "mutagenization")

Deposit Account

The Commissioner is hereby authorized to charge any deficiencies or credit any overpayments in connection with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

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DESIGN OF BETA-SHEET PROTEINS WITH SPECIFIC BINDING PROPERTIES

PATENT CLAIMS

1. Protein with beta-sheet structure,
characterized in that
amino acids exposed on the surface in at least two β-strands exposed on the surface of at least one beta sheet exposed on the surface are specifically mutagenized such that the protein has new or altered specific binding properties or a new or altered catalytic activity or new or altered fluorescence properties.

2. Protein according to Claim 1,
characterized in that
it is included in the group consisting of crystallines, spherulines, heat shock proteins, cold shock proteins, β-helix proteins, lipocalins, certins, fibronectins or transcription factors or is GFP, NGF, tendamistat or lysozyme.

3. Protein according to Claim 1 or 2,
characterized in that,
three beta strands exposed on the surface are mutagenized.

4. Protein according to Claim 1 or 2,
characterized in that,
four or more beta strands exposed on the surface are mutagenized.

5. Protein according one or more of the preceding claims,
characterized in that
at least two beta strands in at least two beta sheets are mutagenized

6. Protein according to one or more of the preceding claims,
characterized in that,
three beta strands in two antiparallel beta sheets are mutagenized.

7. Protein according to one or more of the preceding claims,
characterized in that
it is a crystalline of vertebrates, rodents, birds or fish.

8. Protein according to one or more of the preceding claims,
characterized in that,
it is an alpha-, beta- or gamma-crystalline.

9. Protein according to one or more of the preceding claims,
characterized in that,
it is a gamma-II-crystalline protein.

10. Protein according to one or more of the preceding claims,
characterized in that
the protein is mutagenized in a region of the beta-sheet region accessible to a solvent or to a binding partner.

11. Protein according to one or more of the preceding claims, characterized in that, it is mutagenized in a β-sheet structure of a domain or a subunit of the protein.

12. Protein according to one or more of the preceding claims, characterized in that, it is a gamma-II-crystalline which has been obtained by mutagenesis of one or more of the amino acids Lys 2, Thr 4, Tyr 6, Cys 15, Glu 17, Ser 19, Arg 36 and Asp38 in gamma-II-crystalline.

13. Protein according to one or more of the preceding claims, characterized in that, the protein has been mutagenized in the beta sheet such that it has antibody-like binding properties or an enzymic (catalytic) activity.

14. Protein according to Claim 12 or 13, characterized in that it has binding specificity for estradiol or the conjugate thereof, BSA-β-estradiol-17-hemisuccinate.

15. Protein according to one or more of the preceding claims, characterized in that, it has binding specificity for estradiol or the conjugate thereof, BSA-β-estradiol-17-hemisuccinate and has the following amino acid sequence: cf. Figures 8 and 10.

16. Protein according to one or more of the preceding claims, characterized in that, it is combined with other proteins or non-protein substances.

17. Protein according to one or more of the preceding claims, characterized in that, it has improved binding properties and/or improved catalytic activity and/or improved fluoresence properties.

18. DNA coding for a protein according to one or more of the preceding claims.

19. RNA derived from the DNA according to Claim 18.

20. Prokaryotic or eukaryotic vectors or cells comprising a DNA or RNA according to Claim 18 or 19 or parts thereof coding for functional regions of the protein.

21. Method for preparing a protein according to one or more of the preceding claims, comprising the following steps:

    a. Mutagenesis of the DNA coding for a protein with beta-sheet structure in those regions which code for at least two beta strands, exposed on the surface, of a beta sheet exposed on the surface.

    b. Expression of the mutants obtained in step (a) in a suitable expression system; and

    c. Selection and isolation of mutants having the desired binding properties and/or the desired catalytic activity; optionally

    d. Expression and purification of the beta sheet-mutated proteins.

22. Method according to Claim 21, characterized in that the mutagenesis comprises a mutagenesis of specific amino acid positions (site-specific mutagenesis) or non-specific amino acid positions (random mutagenesis) in the beta sheet.

23. Method according to one or more of the preceding claims, characterized in that, the mutants in step b) are expressed in prokaryotic or eukaryotic cells, in a cell-free system as a complex with ribosomes or on the surface of plant or animal cells, yeast cells or phages, viruses or bacteria.

24. Method according to one or more of the preceding claims, characterized in that mutants having the desired binding properties are selected by contacting these mutants with the binding partner and isolating those mutants having the desired binding affinity.

25. Method according to one or more of the preceding claims, characterized in that mutants having the desired catalytic properties are selected by contacting these mutants with their substrate and isolating those mutants having the desired catalytic activity.

26. Use of a protein according to one or more of the preceding claims in diagnostics and therapy, in cosmetics, bioseparation and biosensors and reduction of harmful substances.